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| 10/573,606 | 03/28/2006 | Jo Klaveness | PN0368 | 6864 |

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| EXAMINER | |
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| PERREIRA, MELISSA JEAN | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Application Number: 10/573,606
Filing Date: March 28, 2006
Appellant(s): KLAVENESS ET AL.

Craig M. Bohlken (Reg. No. 52,628)
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 2/19/08 and 3/11/08 appealing from the Office action mailed 9/24/07.

**(1) Real Party in Interest**

A statement identifying by name the real party in interest is contained in the brief.

**.(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The statement of the status of claims contained in the brief is correct.

**(4) Status of Amendments After Final**

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

**(7) Claims Appendix**

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(8) Evidence Relied Upon**

Marten, K. "Detection of dysplastic intestinal adenomas using enzyme-sensing molecular beacons in mice" Gastroenterology, vol122 (2002), pp406-414

Weissleder, R. "In vivo imaging of tumors with protease-activated near-infrared fluorescent probes" Nature Biotechnology, vol17 (April 1999), pp375-378

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| 6,610,269B1 | Klaveness et al. | 08-2003 |
| 6,008,373 | Waggoner et al. | 12-1999 |

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13,15-18 and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marten et al. (*Gastroenterol.* **2002**, *122*, 406-414) in view of Klaveness et al. (US 6,610,269B1) and further in view of Waggoner et al. (US 6,008,373).

Claims 13,15-18 and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weissleder et al. (*Nature Biotech.* **1999**, *17*, 375-378) in view of

Klaveness et al. (US 6,610,269B1) and further in view of Waggoner et al. (US 6,008,373).

***Response to Arguments***

Applicant's arguments filed 2/19/08 have been fully considered but they are not persuasive.

Appellant asserts that the probes of Marten and Weissleder far exceed the molecular weight limit of 10,000 Daltons of the present claim 13.

The references of Marten and Weissleder were not used to teach of probes having a molecular weight limit of 10,000 Daltons but to teach that cathepsin B cyanine dye probes are used for the imaging of the colon upon cleavage of the poly-L-lysine backbone chain (see figure 1 of Marten and p375 Weissleder). The active probe is thus a smaller segment of the initial Cy5.5 NIRF probe of 35 kDa.

The reference of Klaveness teaches of contrast agents, for imaging colorectal cancer, of formula V-L-R where the vector moiety,V, (peptide), linker moiety, L, (PEG) and detectable reporter moiety may be variable. It is stated that the linker moiety may contain 2-100 recurring units of ethylene oxide having a molecular weight between 120 Daltons to 20 kDaltons. The linker (peptide) and detectable reporter moiety (cyanine dye) of the probes of Klaveness (for imaging colorectal cancer) encompass the linker and detectable reporter moiety of the instant claim 13. Waggoner teaches that the low molecular weight fluorescent probes containing cyanine dyes, linker and proteins have a

greater penetration into cellular environments with molecular weights of 500 to 10000 Daltons.

At the time of the invention it would have been obvious to one skilled in the art to generate a low molecular weight fluorescent probe for imaging colorectal cancer as Waggoner teaches that probes with low molecular weights have a greater penetration into cellular environments and the probes of Marten and Weissleder are active only upon cleavage (reduction of the molecular weight).

Appellant asserts that the fluorochrome probes of Marten and Weissleder accumulates in tumors by slow leakage across highly permeable neovasculature via novel, long, circulating, synthetic graft copolymer. Thus there is no motivation to reduce the molecular weight of the probes of Marten and Weissleder, since those references teach that a high molecular copolymer is an essential part of a successful strategy for tumor imaging.

The fluorochrome probes (cathepsin B cyanine dye probes) of Marten and Weissleder are used for the imaging of the colon upon cleavage of the poly-L-lysine backbone chain (see figure 1 of Marten and p375 Weissleder). The active probe is thus a smaller segment of the initial Cy5.5 NIRF probe of 35 kDa. Also, contrast agents, for imaging colorectal cancer of Klaveness, of formula V-L-R have a variable vector moiety,V, (peptide) linker moiety, L, (PEG) and detectable reporter moiety. It is stated that the linker moiety may contain 2-100 recurring units of ethylene oxide having a molecular weight between 120 Daltons to 20 kDaltons. Waggoner teaches that the low

molecular weight fluorescent probes containing cyanine dyes, linker and proteins have a greater penetration into cellular environments.

At the time of the invention it would have been obvious to generate a low molecular weight fluorescent probe for imaging colorectal cancer as Waggoner teaches that probes with low molecular weights have a greater penetration into cellular environments and the probes of Marten and Weissleder are active only upon cleavage (reduction of the molecular weight). Therefore a low molecular weight fluorescent probe of the combined disclosures will be active upon administration as it doesn't require enzymatic cleavage.

Appellant asserts that Klaveness does not expressly teach that the contrast agent should have a molecular weight below 10,000 Daltons but teaches a wide range of molecular weights for the linker.

The reference of Klaveness teaches of contrast agents, for imaging colorectal cancer, of formula V-L-R where the vector moiety,V, (peptide) linker moiety, L, (PEG) and detectable reporter moiety may be variable. It is stated that the linker moiety may contain 2-100 recurring units of ethylene oxide having a molecular weight between 120 Daltons to 20 kDaltons. The linker (peptide) and detectable reporter moiety (cyanine dye) of the probes of Klaveness (for imaging colorectal cancer) encompass the linker and detectable reporter moiety of the instant claim 13. The reference of Klaveness does not need to expressly teach of the molecular weight below 10,000 Daltons as it is obvious in combination with the reference of Waggoner to vary the linker and vector

moiety to generate a low molecular weight probe to ensure greater penetration into cellular environments.

Appellant asserts that complexes of Waggoner refer to first and second fluorochrome and a linker, not a conjugate with a protein (target material) where the target material is something additional to the complex. Appellant asserts that Waggoner is silent on the molecular weight of the species containing a target material.

The reference of Klaveness teaches of contrast agents, for imaging colorectal cancer, of formula V-L-R where the vector moiety,V, (peptide) linker moiety, L, (PEG) and detectable reporter moiety may be variable. It is stated that the linker moiety may contain 2-100 recurring units of ethylene oxide having a molecular weight between 120 Daltons to 20 kDaltons. The linker (peptide) and detectable reporter moiety (cyanine dye) of the probes of Klaveness (for imaging colorectal cancer) encompass the linker and detectable reporter moiety of the instant claim 13. The reference of Waggoner to vary the linker and vector moiety to generate a low molecular weight probe to ensure greater penetration into cellular environments.

At the time of the invention it would have been obvious to generate a low molecular weight fluorescent probe for imaging colorectal cancer (of Klaveness) by varying the linker, vector and detectable reporter moieties as Waggoner teaches that probes with low molecular weights have a greater penetration into cellular environments. Also, the probes of Marten and Weissleder are active only upon cleavage (reduction of the molecular weight). Therefore a low molecular weight

fluorescent probe of the combined disclosures will be active upon administration as it doesn't require enzymatic cleavage.

Appellant asserts that the reference of Waggoner is not even of the same utility as the present invention, since it is silent on both in vivo imaging and contrast agents. T

The secondary reference of Waggoner does not need to address the same utility or address the same problems as the instant claims. The references are all drawn to fluorescent complexes comprising a linker and a vector moiety.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Melissa Perreira/

Examiner, Art Unit 1618

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